ACCOMPANYING DOCUMENTS

Accompanying this response are the following documents: an information disclosure statement under 37 C.F.R. §1.97(c), form PTO-1449, and copies of the cited references.

REMARKS

Introductory Comments:

Claims 1-40 are currently pending and were examined as discussed in the Office Action dated 8 August 2000. In the subject Office Action, the following rejections were raised: **(1)** claims 1-40 were rejected under 35 U.S.C. §101 as claiming the same invention as that of copending U.S. Patent Application No. 09/235,944; **(2)** claims 1-32 were rejected under 35 U.S.C. §112, first paragraph as nonenabled; **(3)** claims 1-4, 11-12, 17, 19, 20-23 and 27 were rejected under 35 U.S.C. §103(a) as unpatentable over U.S. Patent No. 5,630,796 to Bellhouse et al. ("Bellhouse"); and **(4)** claims 1-40 were rejected under 35 U.S.C. §103(a) as unpatentable over Bellhouse in view of U.S. Patent No. 5,962,477 to Mak ("Mak"). These rejections are traversed for the following reasons.

The Provisional Double-Patenting Rejection

Claims 1-40 have been provisionally rejected under 35 U.S.C. §101 as claiming the same invention as that of claims 1-40 of copending Application No. 09/235,944. The rejection is provisional since the conflicting claims have not in fact been patented.

In response, applicants note that their copending application has now been abandoned, thereby obviating the instant provisional double-patenting rejection. Reconsideration and withdrawal of the rejection is respectfully requested.

The Rejection under 35 U.S.C. §112, first paragraph:

Claims 1-32 stand rejected under 35 U.S.C. §112, first paragraph, as nonenabled. In particular, the Office asserts that "claim 1 recites 'a first transdermal drug delivery device' which means there is a second transdermal drug system, however no second drug delivery system is recited in the claim." The Office thus concludes "the claims are nonenabling unless the limitation of claim 14 is included in the independent claim 1." Applicants respectfully traverse.

Applicants' obligation under 35 U.S.C. §112, first paragraph, is to provide a specification that contains sufficient disclosure so as to enable the ordinarily skilled artisan to make and use the claimed invention throughout its scope. In providing this disclosure, and in selecting the claim language with which to define their invention, applicants are entitled to be their own lexicographer. Thus, when selecting the language of claim 1, applicants choose to recite in part (b) the use of either a "first transdermal drug delivery device" or a "first occlusive dressing" that is positioned over the predetermined (target) area of skin or mucosa where the therapeutic agent is administered. The descriptor "first" was selected to provide antecedence and clarity for a subsequent claim (claim 14) wherein a pretreatment step has now been introduced, and this new step entails the use of a "second transdermal delivery device" or a "second occlusive dressing." This new pretreatment step is not an essential part of the base claims (claims 1, 11 and 13) and as such applicants have no obligation to insert said pretreatment step into claim 1 as requested by the Office. This new pretreatment step is further carried out using either a transdermal delivery device or an occlusive dressing that is different and discrete from the transdermal delivery device or occlusive dressing used in the "treatment" step (part b) of the claim. Accordingly, the devices used in the pretreatment step are recited differently (i.e., as "second") in claim 14.

Applicants submit that the skilled artisan, upon reading applicants' specification and claims, is fully enabled to make and use the recited invention throughout its scope. The use of the descriptor "first" in claim 1 does not necessitate the recitation of "second," "third," etc. devices in the base claim, rather, the use of this

term provides both antecedence and clarity for the entire claim set when it is considered as a whole and in light of the enabling disclosure found in applicants' specification. Applicants can think of no basis for the Office's requirement in either Section 112, in the rules (37 C.F.R.), or in the M.P.E.P.. Should the Office decide to maintain this rejection, applicants respectfully request clarification of the Office's grounds for the rejection.

For these reasons, then, applicants submit that the rejection of claims 1-32 under 35 U.S.C. §112, first paragraph, is improper. Reconsideration and withdrawal of the rejection is thus respectfully requested.

The Rejections under 35 U.S.C. §103:

Claims 1-4, 11-12, 17, 19, 20-23 and 27 were rejected under 35 U.S.C. §103(a) as unpatentable over the disclosure of Bellhouse. The Office asserts that Bellhouse "teaches a needleless syringe for effective transdermal delivery of particles containing a therapeutic agent." Although the Office acknowledges that "[Bellhouse] does not teach topically positioning a transdermal drug delivery device or occlusive dressing comprising the therapeutic agent," the Office nonetheless concludes that "it is obvious .. to dress the site of the injection with an occlusive dressing or transdermal device after injection as a routine technique." The Office asserts that "the teaching of [Bellhouse] that more than one therapeutic agents can be delivered together," or that the "particles are coated to control permeability" provides sufficient basis for this conclusion. Applicants respectfully disagree.

Section 2143 of the M.P.E.P. sets forth the following three basic requirements for *prima facie* obviousness: (1) there must be some suggestion or motivation to modify or combine the references; (2) there must be a reasonable expectation of success for the modification and/or combination; and (3) the prior art reference must teach or suggest all the claim limitations. When assessing these issues, (1) the claimed invention must be considered as a whole; (2) the references must be considered as a whole and must suggest the desirability of making the combination; (3) the references must be viewed without the benefit of impermissible hindsight; and

(4) a reasonable expectation of success is the standard with which obviousness is determined. *Hodosh v. Block Drug Co., Inc.*, 229 USPQ 182, 187, n.5 (Fed. Cir. 1986). Applicant submits that the Office has failed to satisfy these criteria, and has thus failed to establish *prima facie* obviousness over the Bellhouse reference.

In order to properly assess the instant obviousness determination, applicant's claimed invention must be considered as a whole. Turning to claim 1, the "whole" of the claimed subject matter is: a method for administering a therapeutic agent to a predetermined area of skin or mucosa. The method comprises two steps, a first step of accelerating particles into the skin or mucosal target, and a second step of positioning a transdermal delivery device or occlusive dressing over the same area. The particles, or the transdermal delivery device, or the occlusive dressing, or any combination thereof will comprise the therapeutic agent to be delivered using the claimed method.

Applicants have found, surprisingly, that such a combination of techniques provides for synergistic, beneficial delivery effects. For example, when the first step is used to deliver placebo particles (i.e., the therapeutic agent is not included in the particles), applicants have found that these placebo particles actually establish temporary delivery channels in the outer skin layer, such that delivery of a therapeutic agent from an occlusive dressing or transdermal delivery system placed over the these delivery channels is greatly enhanced. Alternatively, when the first step is used to deliver therapeutic particles, applicants have found that the provision of an occlusive dressing over the particle delivery site significantly enhances flux of the therapeutic agent (this enhanced delivery occurs despite the fact that the occlusive dressing contains no further therapeutic agent. Combined deliveries, wherein the therapeutic agent is delivered with both steps, likewise provides synergistic delivery effects and further allows for custom tailoring of delivery profiles using the unique delivery characteristics of each system employed in the method.

The combination of steps (a) and (b) represents the "whole" of the claimed method, not the discrete parts. It is accordingly this particular recited combination of elements that must be compared--as a whole--against the cited prior art. It is also,

therefore, the Office's burden to establish that, *prima facie*, this particular recited combination was suggested by the prior art (considering the prior art as a whole for what it fairly teaches the skilled artisan), the prior art suggested the desirability of making the combination, and that there was a reasonable expectation of success for the suggested combination. Applicants submit that the Office has not met this burden.

Turning to the Office's basis for the rejection, applicants note that the Office asserts that Bellhouse teaches transdermal delivery of powdered therapeutic agents using a needleless syringe, but acknowledges that Bellhouse does not teach applicants' recited combination, that is, that Bellhouse fails to teach any process that combines disparate delivery elements in a two step process to enhance (or even create a new) therapeutic delivery profile. To relate this back to the whole of applicants' recited method, the Office has merely shown that Bellhouse teaches a single, discrete element of one possible combination under applicants' claims (i.e., that a therapeutic agent can be delivered in applicants' step (a)), but fails to teach applicants' particular combinations, much less the desirability of using any combination. In other words, the Office has failed to show that applicants' particular recited combination was taught or suggested by the prior art (Bellhouse). This is because applicants' claimed invention simply was not obvious.

For example, where in Bellhouse does the Office find the teaching or suggestion that their needleless syringe could be used to deliver inert, inactive (placebo) particles providing no therapeutic agent whatsoever, and further that this placebo delivery should be conducted in combination with a different delivery system? Where in the Bellhouse reference would one look to find the teaching or suggestion that transdermal patches, or occlusive devices should be combined with the therapeutic particle delivery methodology to provide for enhanced or altered therapeutic effect? Applicants submit that such disclosures simply cannot be found in Bellhouse, nor in the prior art considered fairly and as a whole. The Office's assertions that occlusive dressings or transdermal devices are "routine techniques" does not make up for this utter lack of disclosure. In like manner, the Office's assertions that the requisite teaching of applicants' particular recited combination

somehow flows from Bellhouse's disclosure that several particulate therapeutic agents can be delivered together, or that the therapeutic particles can be coated to enhance penetration or control release simply defies logic. To paraphrase the Federal Circuit, it is improper to assert that the existence of a unicorn was obvious after taking a trip to the zoo and seeing a horse and a white rhinoceros in adjacent cages--it takes a spark of inventiveness to look at a horse and then look at a white rhinoceros and then conceive the idea of a white horse with a horn on its nose. What the Office has done is look at the horse (Bellhouse), conjure up some rhinoceros (the existence of "routine techniques" in the prior art) and then somehow divine that applicants' recited combination was obvious. There is simply no requisite suggestion or teaching from the prior art to carry out this modification of Bellhouse and arrive at applicants' particular combination. The mere existence of one element of but one possible combination (Bellhouse's delivery of powdered therapeutics) in the prior art does not provide the requisite motivation or teaching to arrive at applicants' cited combination.

For al of the foregoing reasons, applicants submit that the Office has failed to show that, *prima facie*, applicants' particular recited combination was suggested by the prior art (considering Bellhouse and the rest of the prior art as a whole for what was fairly taught to the skilled artisan). The Office has further failed to show that, *prima facie*, Bellhouse or any other prior art disclosure suggested the desirability of making applicants' recited combination. Since neither the particular combination, nor the desirability of making that combination was taught or suggested by the prior art, there cannot have been a reasonable expectation of success for the combination. Something that is unknown, not taught and not suggested cannot possibly enjoy a reasonable expectation for success.

Accordingly, the rejection of claims 1-4, 11-12, 17, 19, 20-23 and 27 under 35 U.S.C. §103(a) as unpatentable over the disclosure of Bellhouse is deemed improper and simply not supported by the cited art. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

Claims 1-40 stand rejected under 35 U.S.C. §103(a) as unpatentable over the combination of Bellhouse in view of Mak. In particular, the Office asserts that Mak

"teaches formulation for topical administration of therapeutic agents [in various forms]" and that these agents can be delivered using "active or passive transdermal patch[es], occlusive dressing[s] or transmucosal delivery device and absorption enhancer[s]." The Office further asserts that an "occlusive dressing [is] optionally applied to the skin after [application of] the therapeutic agent ... pretreatment of [an] area of skin upon which drug is to be placed prior to [application] of the transdermal patch ... [and] use of two separate dosage forms at the same time," referring to several specific sections of the Mak reference. The Office then concludes it would have been obvious to use the Bellhouse needleless syringe after pretreatment with the transdermal patches of Mak and then apply a further transdermal device containing the same or different drug. Applicants respectfully disagree.

As discussed above, the primary reference to Bellhouse fails to teach or suggest applicants' recited combinations. The addition of Mak as a secondary reference does not make up for this shortcoming.

Turning now to the Mak reference, applicants strongly disagree with the Office's characterization of what the Mak fairly teaches to the skilled artisan when that reference is considered as a whole as indeed it must be under a Section 103 analysis. What Mak teaches is that certain therapeutic agents can be used to modulate or prevent inflammatory/immune conditions. Mak describes numerous such agents, all having anti-inflammatory properties (see columns 29-42 inclusive). Mak teaches that these agents can be used to treat local or systemic inflammatory events, and that such agents can even be used to reduce inflammation events occurring as a result of traditional transdermal delivery devices (application of such patches to the skin can create irritation, inflammation and/or sensitization that is not beneficial). Mak teaches that these agents can be delivered using numerous delivery techniques known in the art, and that agents can be combined.

However, when one assesses what Mak fairly teaches to one of skill in the art, either looking at the reference as a whole or even considering just the specific tidbits and incomplete portions of the Mak disclosure expressly identified by the Office (see page 5 of the Office Action), one does not find any teaching or suggestion of

applicants' particular recited combination, that is, the use of a particle delivery system in specific combinations with occlusion and/or transdermal delivery techniques to enhance drug delivery or establish a drug delivery profile simply not possible with any of the individual drug delivery systems. In addition, one cannot find anywhere in Mak any teaching or suggestion that placebo particles could be accelerated through a skin or mucosal site to facilitate drug delivery from an occlusive dressing or transdermal drug delivery device. Particle delivery techniques form a unique and necessary portion of every recited combination covered by applicants' claims.

Since neither Bellhouse nor Mak, alone or in any conceivable combination, teaches or suggests applicants' recited combination, the only way to arrive at this particular unique combination is through applicants' own disclosure which is simply not available as prior art. More particularly, since there is simply no suggestion or motivation that has been identified in the cited art that would lead one to applicants' claimed invention, the only way to arrive at the Office's conclusion of obviousness is to piece together bits and pieces of the prior art using the template provided by applicants' own specification. This hindsight reconstruction of applicants' invention is improper.

For all of the foregoing reasons, then, applicants submit that the rejection of claims 1-40 under 35 U.S.C. §103(a) is improper. The Office has failed to identify in the prior art the requisite teaching or suggestion to arrive at applicant's claimed invention when it is considered as a whole as it must be under a Section 103 analysis. The Office has failed to establish a *prima facie* showing of obviousness over its cited combination since: (a) it has not identified, in the prior art, the requisite suggestion or motivation to modify or combine these references in such a way as to arrive at applicants' unique combination; (b) it has also failed to identify in the prior art the requisite teaching of the desirability to modify or combine these references and arrive at applicant's invention; and (c) there cannot have been a reasonable expectation of success for such a modification and/or combination since it was neither taught nor suggested by the prior art. When Bellhouse and Mak are considered as a whole and viewed without the benefit of impermissible hindsight, it is clear that they simply fail

to teach or suggest the desirability of making applicants' recited combination, and much less the actual combination. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

CONCLUSION

Applicants submit that the claims define an invention which is both novel and nonobvious over the prior art. Accordingly, a Notice of Allowance is believed in order and the issuance of such a notice is respectfully requested. Applicants further ask that, should the Examiner note any remaining issues that may be resolved with a telephone call, that she contact the undersigned at (510) 742-9700, ext. 209.

Respectfully submitted,
POWDERJECT TECHNOLOGIES, INC.

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By: _____
Thomas P. McCracken
Registration No. 38,548

6511 Dumbarton Circle
Fremont, CA 94555
Telephone: (510) 742-9700, ext. 209
Fax: (510) 742-9720